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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,689	08/11/2005	Masateru Yamada	0760-343PUS1	8519

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

NOTIFICATION DATE	DELIVERY MODE
11/16/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,689	YAMADA ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *11-16 and 19-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☒ Claim(s) *9,10,17,18,27 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/2005 11/6/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 8/27/2007.

Claims 1-28 are currently pending ad are addressed herein.

Election/Restrictions

1. Applicant's election with traverse of Group I and the species antisense oligonucleotide and SEQ ID NO: 1 in the reply filed on 8/27/2007 is acknowledged. The traversal is on the ground(s) that (1) it would not be an undue burden to search all claims, and (2) although lack of unity of invention should certainly be raised in clear cases, it should neither be raised nor maintained on the basis of a narrow, literal or academic approach and there should be a broad, practical consideration of the degree of interdependence of the alternatives presented.

This is not found persuasive because (1) the claims are restricted under PCT Rule 13.1 and 13.2 as this is the national stage entry of an international application and in such cases search burden is not a consideration, only unity of invention, and (2) in the instant case, there is clearly no unity of invention because the technical feature linking the inventions was known in the prior art, as previously indicated. In order for unity of invention to exist the inventions must be linked by a special technical feature. A special technical feature must make a significant contribution over the prior art. In other words, technical features which are not novel cannot be special technical features. Thus in this case, there is no special technical feature linking the inventions, as the technical feature linking the claims (i.e., an agent that inhibits casing kinase 2) was known in the prior art as indicated in the previous action and as indicated herein.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 11-16 and 19-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/27/2007.

3. Claims 1-10, 17, 18, 27 and 28 are examined herein.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on 7/20/2005 and 11/6/2006 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Objections

Claims 9, 10, 17, 18, 27 and 28 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits. Specifically, claims 9 and 10 depend on claims 7 or 8 which depend on claim 4 which depends on any one of claims 1 to 3; claims 17 and 18 depend on any one of claims 1-16 while claim 4 depend on any one of claims 1-3; and claims 27 and 28 depend on claim 26 which depends on any one of claims 21-25 while claim 25 depends on any one of claims 21-23.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication No. 2004/0126784 A1 (Hitoshi et al.).

7. The instant claims encompass an antisense oligonucleotide which targets the mRNA and inhibits expression of casein kinase 2, wherein the antisense oligonucleotide is 12-50 nucleotides in length and wherein the oligonucleotide is an S-oligonucleotide (i.e., as Si-nucleotide).

8. Hitoshi et al teach an SiRNA molecule (i.e., an S-oligonucleotide) which is an antisense oligonucleotide which targets the mRNA and inhibits expression of casein kinase 2 and wherein the antisense oligonucleotide has a length in the range of 12-50 nucleotides. Specifically, see paragraph [0011]. Therefore, Hitoshi et al. clearly anticipates the instant claims.

9. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Formby et al. (Molec. Cell. Biochem. 1998, vol 187, pages 23-31).

The instant claims encompass an antisense oligonucleotide which targets the mRNA and inhibits expression of casein kinase 2, wherein the antisense oligonucleotide is 12-50 nucleotides in length.

Formby et al. teach an antisense oligonucleotide which targets the mRNA and inhibits expression of casein kinase 2 and wherein the antisense oligonucleotide has a length in the range of 12-50 nucleotides. Specifically see abstract; page 24 under "Antisense oligonucleotides"; page 25, second column; Figures 2-4; etc.).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-8 rejected under 35 U.S.C. 103(a) as being unpatentable over Formby et al. (Molec. Cell. Biochem. 1998, vol 187, pages 23-31) as applied to claims 1-6 above, and further in view of Bass (*Nature* 2001, vol. 411 pages 428-429) and Tuschl et al. (US Patent Application Publication No. 2004/0259247 A1.

As indicated above, Formby et al. teach an antisense oligonucleotide which targets the mRNA and inhibits expression of casein kinase 2 and wherein the antisense oligonucleotide has a length in the range of 12-50 nucleotides. Specifically see abstract; page 24 under "Antisense oligonucleotides"; page 25, second column; Figures 2-4; etc.).

Formby does not teach that the antisense oligonucleotide is an S-oligonucleotide (e.g., a SiRNA).

However, it would have been prima facie obvious to one of skill in the art at the time of the invention to use siRNA in place of antisense oligonucleotides to inhibit the expression of casein kinase 2 for the following reasons.

Bass taught that, like some antisense oligonucleotides, which trigger RNase H-catalyzed cleavage of their targets, siRNAs trigger the degradation of complementary messenger RNAs (page 428 and Fig. 1). A general outline of the RNAi mechanism is taught, showing how siRNA-mediated RNAi may be used to interfere with gene expression using siRNAs directed against specific mRNA sequences (Fig. 1). Bass teaches that RNAi has repeatedly proven itself to be more robust than antisense techniques: it works more often, and typically decreases expression of a gene to lower levels, or eliminates it entirely. Furthermore, siRNAs are effective at

concentrations that are several orders of magnitude below the concentrations typically used in antisense experiments. Thus, Bass directly compares and contrasts antisense and RNAi technologies for use in gene expression inhibition.

Tuschl et al. taught methods and materials for making and using short double-stranded RNA molecules for inhibiting the expression of virtually any known gene in mammalian cells via RNA interference (paragraphs 10, for example). Tuschl et al. teach that, to avoid triggering the interferon response in mammalian cells, one should use short, 21-nt, dsRNAs, or siRNAs. Tuschl et al. show that siRNAs may be used to selectively suppress the expression of specific endogenous and heterologous genes in different mammalian cell lines, including HeLa cells, without triggering the interferon response (paragraph 34).

Importantly, Tuschl et al. also compare and contrast siRNA methodology to that of antisense and ribozyme techniques for inhibiting gene expression. At paragraph 148, for example, Tuschl et al. state that siRNAs are extraordinarily powerful reagents for mediating gene silencing and that siRNAs are effective at concentrations that are several orders of magnitude below the concentrations applied in conventional antisense or ribozyme gene targeting experiments. At paragraph 137, Tuschl et al. state that the remarkable finding that synthetic 21 and 22 nt siRNA duplexes can be used for efficient mRNA degradation provides new tools for sequence-specific regulation of gene expression in functional genomics as well as biomedical studies. The siRNAs may be effective in mammalian systems where long dsRNAs cannot be used due to the activation of the PKR response. As such, the siRNA duplexes represent a new alternative to antisense or ribozyme therapeutics.

Tuschl et al. provides a complete blueprint for the design, synthesis, and application of modified and unmodified siRNAs against virtually any known gene. A number of different working examples, showing sequence-specific, reproducible knockdown of different transgenes and endogenously expressed genes in mammalian cells, using structurally defined siRNAs are shown (see Examples 1-3). It is taught that siRNAs are extraordinarily powerful reagents for mediating gene silencing, and that siRNAs are effective at concentrations that are several orders of magnitude below the concentrations applied in conventional antisense or ribozyme gene-targeting experiments (paragraph 148).

Thus, the prior art taught, in general, that siRNAs and antisense oligonucleotides can be used to produce the same effect, albeit with different potencies and by different biochemical mechanisms. siRNAs and antisense oligos can both be used to inhibit gene expression *in vivo* or *in vitro*, via mRNA degradation or translation attenuation, and, thus, both types of nucleic acids may be used to prevent the expression of a gene in a cell. For example, Bass teaches that antisense RNA is another technique to prevent the expression of particular genes (page 429). Thus, in this sense, siRNAs and antisense oligos are art-recognized equivalents that may be used for the same purpose: reducing or inhibiting gene expression. (See for example MPEP §2144.06, SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE.)

Furthermore, it would have been prima facie obvious to one of ordinary skill in the art, at the time the invention was made, to make S-oligonucleotides, or more specifically, siRNAs, as taught by Tuschl et al. and Bass, for inhibition of casein kinase 2 gene expression in cells, as taught by Formby et al. with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to make an SiRNA as a substitute for an antisense oligonucleotide to inhibit casein kinase 2 expression because the prior art teaches that siRNAs possess certain advantages over antisense oligos (e.g., see Baker and Tuschl).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner
Art Unit 1635